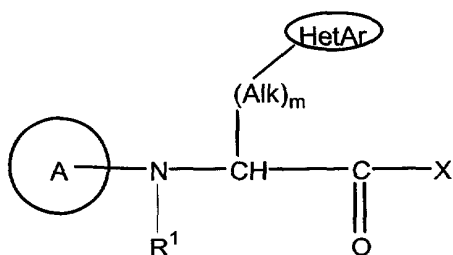


**WHAT IS CLAIMED IS:**

1. A compound of Formula (I):



(I)

wherein:

- A is an aryl, heteroaryl, cycloalkyl, or heterocyclic group wherein said aryl, heteroaryl, cycloalkyl, or heterocyclic group is optionally substituted, on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen, hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, -OS(O)<sub>2</sub>-alkyl, -OS(O)<sub>2</sub>-substituted alkyl, -OS(O)<sub>2</sub>-aryl, -OS(O)<sub>2</sub>-substituted aryl, -OS(O)<sub>2</sub>-heteroaryl,

-OS(O)<sub>2</sub>-substituted heteroaryl, -OS(O)<sub>2</sub>-heterocyclic, -OS(O)<sub>2</sub>-substituted heterocyclic, -OSO<sub>2</sub>-NRR where each R is independently hydrogen or alkyl, -NRS(O)<sub>2</sub>-alkyl, -NRS(O)<sub>2</sub>-substituted alkyl, -NRS(O)<sub>2</sub>-aryl, -NRS(O)<sub>2</sub>-substituted aryl, -NRS(O)<sub>2</sub>-heteroaryl, -NRS(O)<sub>2</sub>-substituted heteroaryl, -NRS(O)<sub>2</sub>-heterocyclic, -NRS(O)<sub>2</sub>-substituted heterocyclic, -NRS(O)<sub>2</sub>-NR-alkyl, -NRS(O)<sub>2</sub>-NR-substituted alkyl, -NRS(O)<sub>2</sub>-NR-aryl, -NRS(O)<sub>2</sub>-NR-substituted aryl, -NRS(O)<sub>2</sub>-NR-heteroaryl, -NRS(O)<sub>2</sub>-NR-substituted heteroaryl, -NRS(O)<sub>2</sub>-NR-heterocyclic, -NRS(O)<sub>2</sub>-NR-substituted heterocyclic where R is hydrogen or alkyl, -N[S(O)<sub>2</sub>-R']<sub>2</sub> and -N[S(O)<sub>2</sub>-NR']<sub>2</sub> where each R' is independently selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

HetAr is a nitrogen containing heteroaryl or a nitrogen containing substituted heteroaryl group;

Alk is an alkylene group of 1 to 4 carbons;

*m* is 0 or 1;

R<sup>1</sup> is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenoxo, substituted cycloalkenoxo, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy and -NR''R'' where each R'' is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof;

and further wherein the compound of Formula (I) has a binding affinity to VLA-4 as expressed by an  $IC_{50}$  of about  $15\mu M$  or less.

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2. The compound of Claim 1 wherein HetAr is a nitrogen containing substituted heteroaryl group.

3. The compound of Claim 1 wherein HetAr is a nitrogen  
10 containing heteroaryl group that is substituted with a substituent selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino  
15 oxysulfonyl, aryl and substituted aryl.

4. The compound of Claim 1 wherein HetAr is a nitrogen  
containing heteroaryl group is substituted with a group of formula  $-O-Z-NR^{11}R^{11'}$  or  $-O-Z-R^{12}$  wherein  $R^{11}$  and  $R^{11'}$  are independently selected from  
20 the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where  $R^{11}$  and  $R^{11'}$  are joined to form a heterocycle or a substituted heterocycle,  $R^{12}$  is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from  
25 the group consisting of  $-C(O)-$  and  $-SO_2-$ .

5. The compound of Claim 4 wherein the nitrogen containing heteroaryl group is substituted with a group of formula  $-OC(O)NR^{11}R^{11'}$  wherein  $R^{11}$  and  $R^{11'}$  are independently selected from the group consisting of

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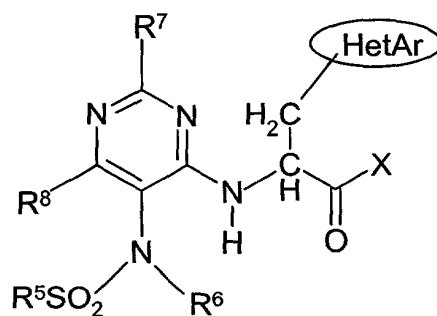
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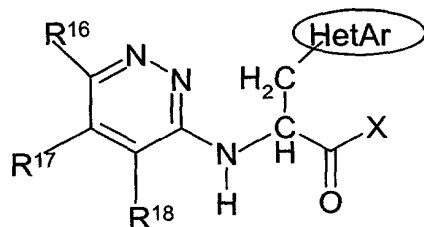
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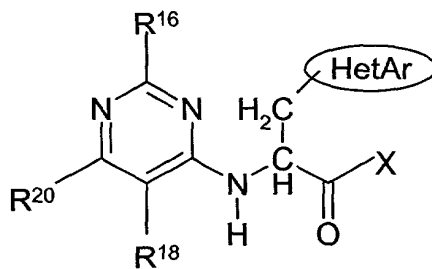
11. The compound of Claim 1 wherein the compound has formula  
IIa, IIb, IIc, IId, or IId:



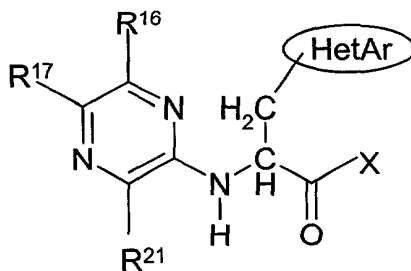
IIa



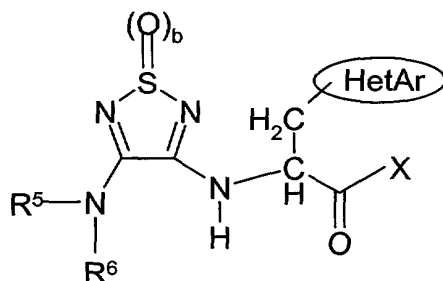
IIb



IIc



IIId,



IIe

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wherein:

HetAr is a nitrogen containing heteroaryl group substituted with a  
 substituent selected from the group consisting of acyl, acylamino, acyloxy,  
 10 aminoacyl, aminocarbonylamino, aminothiocabonylamino,  
 aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino,  
 thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl,  
 oxysulfonylamino, aryl, substituted aryl, and oxysulfonyl;

R<sup>5</sup> is selected from the group consisting of alkyl, substituted alkyl,  
 15 alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted

cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

$R^6$  is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and  $-SO_2R^{10}$  where  $R^{10}$  is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

$R^7$  and  $R^8$  are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

$R^{16}$  and  $R^{17}$  are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

$R^{18}$  is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

$R^{20}$  is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

$R^{21}$  is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

$b$  is 1 or 2; and

X is hydroxyl; and  
and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

5           12.    The compound of Claim 11 wherein the compound is selected from formula IIc, IId or IId.

10           13.    The compound of Claim 11 or 12 wherein HetAr is a nitrogen containing heteroaryl group which is substituted with a group of formula -O-Z-NR<sup>11</sup>R<sup>11'</sup> or -O-Z-R<sup>12</sup> wherein R<sup>11</sup> and R<sup>11'</sup> are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R<sup>11</sup> and R<sup>11'</sup> are joined to form a heterocycle or a substituted heterocycle, R<sup>12</sup> is selected from the group  
15           consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO<sub>2</sub>-.

20           14.    The compound of Claim 13 wherein the nitrogen containing heteroaryl group is substituted with a group of formula -OC(O)NR<sup>11</sup>R<sup>11'</sup> wherein R<sup>11</sup> and R<sup>11'</sup> are independently selected from the group consisting of alkyl or R<sup>11</sup> and R<sup>11'</sup> are joined to form a heterocycle or a substituted heterocycle.

25           15.    The compound of Claim 14 wherein the nitrogen containing heteroaryl group is substituted with -OC(O)N(CH<sub>3</sub>)<sub>2</sub> and is at the para position of the heteroaryl group.

30           16.    The compound of Claim 11 or 12 wherein HetAr is a nitrogen containing heteroaryl group which is substituted with an aryl or substituted aryl group.



17. A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claims 1 to 16.

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18. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claims 1-16.

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